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# SYNTHESIS PAPER

entitled

## *QUANTIFICATION OF THE CHEMICAL BOND WITHIN ORTHOGONAL SPACES OF REACTIVITY. APPLICATIONS ON MOLECULES OF BIO-, ECO- AND PHARMACO-LOGICAL INTEREST*

including the work done and the results obtained in relation to the objectives achieved during the research grant

**CNCSIS TE/16/2010-2013, Contract 94 of 03.08.2010**

on year 2010.

## Preamble

The computational chemistry, in general, with the specializations computational (eco)toxicology and molecular design, represents a priority field of research also found in research program of European Commission. This because allows the prediction, in real time, of the reactive potential, of specific bonding, and toxicology that a substance newly synthesized can have on some bimolecules (usually proteins) found in organisms from the bio- or eco- sphere. Moreover, by the molecular design can be modeled and predicted *in silico* the structure of a molecule still unsynthesized, but required in order to activate or inhibit various molecular processes or metabolic with eco-, bio- or pharmaco- logical impact. Yet, on the basis of these implementations and molecular projections stay the fundamental principles of the quantum chemistry, as long as the interactions involved are of quantum-spherical type, the phenomenon of electronic and protonic tunneling of the barriers of potential intra- and inter- molecular being determinant for the formation of the chemical bonds with high degree of specificity, on enzyme-substrate type or receiver-ligand. In this context, the present project aims the advancement, the implementation and the application of a new mechanism of quantum interaction at molecular level: the modeling of the quantum bond in orthogonal (algebraic) spaces – in general, and of the indices of reactivity (electronegativity, chemical hardness and action) calculated inside the density functional theory- in particular. By applying the consecrated principles of reactivity (the equalization of electronegativity, acids and bases, strong and soft, the maximum chemical hardness of the bimolecular fragments) but also of the recent variational principle of the chemical action (Putz, 2007) in various quantum configurations of reactivity is performed the quantitative-qualitative analyze of the specific interaction by the orthogonal chemical bond, generalizing the frequently used paradigm l-dimensional of the chemical modeling in the reaction coordinate.

## Objectives and Results

1. **Was promoted the idea of an algorithm Double-QSAR to improve the performances of correlation of the classical method *(papers [1- 4])*.**

The main idea is to effectuate the so-called double-variations in the total energy of a chemical system, with the expression obtained in the context of the density functional theory [1]

$$\delta[dE] = -\delta[\chi dN] + \delta[\eta (dN)^2] + \int \delta[\rho(\mathbf{r}) dV(\mathbf{r})] d\mathbf{r}$$

wherefrom, by the coupling with the reactivity condition (aka the equivalent of entropic increase)

$$\delta[dE] \geq 0$$

for a not-null charge transfer, but constant, and a not-null fluctuation in the external potential applied

$$dN = |dN| = ct. \neq 0,\ dV(\mathbf{r}) \neq 0$$

unitary, are obtained:

- variational principle of electronegativity (that contains both the equalization of the electronegativity and its residual fluctuation) $\delta[\chi] \leq 0$
- variational principle of the chemical hardness (that integrates the principles of the hard and soft acids and bases- HSAB and of the maximum chemical hardness) $\delta[\eta] \geq 0$
- with the recent advanced principle of the chemical action that represents a typical principle of global optimization of the reactivity

$$\delta C_A = 0,\ C_A = \int \rho(\mathbf{r}) V(\mathbf{r}) d\mathbf{r}$$

in terms of the electronic density of the system and of the external potential applied.

Thus, transferred in QSAR analyze (quantitative structure-activity relationship), the principle of the double variations was explained in the evaluation of the equations, in the first instance, of the chemical aromaticity as multilinear functions of forms of the electronegativity and chemical hardness. Was found that, indeed, for a typical set of compounds (46 hydrocarbons) and the evaluation in spectral like resolution conditions (SLR) of in the regime of the finite difference in scheme 10-pentagonal (10-P) is obtained a formula QSArR (quantitative structure-aromaticity relationship) with a high truth value, i.e. [2]

$$A = 373.7334 + 161.667\eta_{SLR} + 106.8799\chi_{SLR} - 174.3477\eta_{10P}$$

for the statistical factors

$$SEE = 26.9, F = 272.0, R^2 = 0.9499, R^2_{CV} = 0.9224$$

The value of this approach justifies the consideration of the electronegativity and the chemical hardness to be considered as indicators of the reactivity/chemical stability in an orthogonal space, these being considered strongly independent on the QSArR studies associated. Thus, formally, a „velocity-acceleration" space

$$\mathbf{v} = \frac{\partial \mathbf{r}}{\partial t} \leftrightarrow \frac{\partial E}{\partial N} = -\chi,$$

$$\mathbf{a} = \frac{\partial \mathbf{v}}{\partial t} \leftrightarrow \frac{\partial^2 E}{\partial N^2} = 2\eta$$

in reactivity can be considered, as a first instance, as being associated with the electronegativity-chemical hardness space, for fundamental approached and applications [3,4].

## 2. Was generalized the space of quantum evolution by the extension of the relation of indetermination of Heisenberg *(papers [5-10])*.

With a great value for the quantum theory in general, but also for the quantum-chemical in particular, were materialized the results of the complete study of the free quantum evolution +

observed (through experiment) in relation with the principle of Heisenberg indetermination. Thus, was concluded the general form of revised Heisenberg uncertainty (see Figure 1) [5]

$$\Delta x \Delta p \geq \frac{\hbar}{2}\sqrt{1-n^2},$$

depending on the so-called factor of quantum fluctuation

$$n \in [0,1]$$

that can pe evaluated for each individual experiment, using the formula

$$n = \sqrt{\frac{\left\langle x_0^2 \right\rangle_{Exp}}{\left| \left\langle x^2 \right\rangle_{Exp} - \left\langle x_0^2 \right\rangle_{Exp} \right|}}$$

that contains information about the average of the initial position-prepared ($x_0$) as like as of the observed one ($x$) as a result of the free-evolution (quantum interaction) of the system in cause

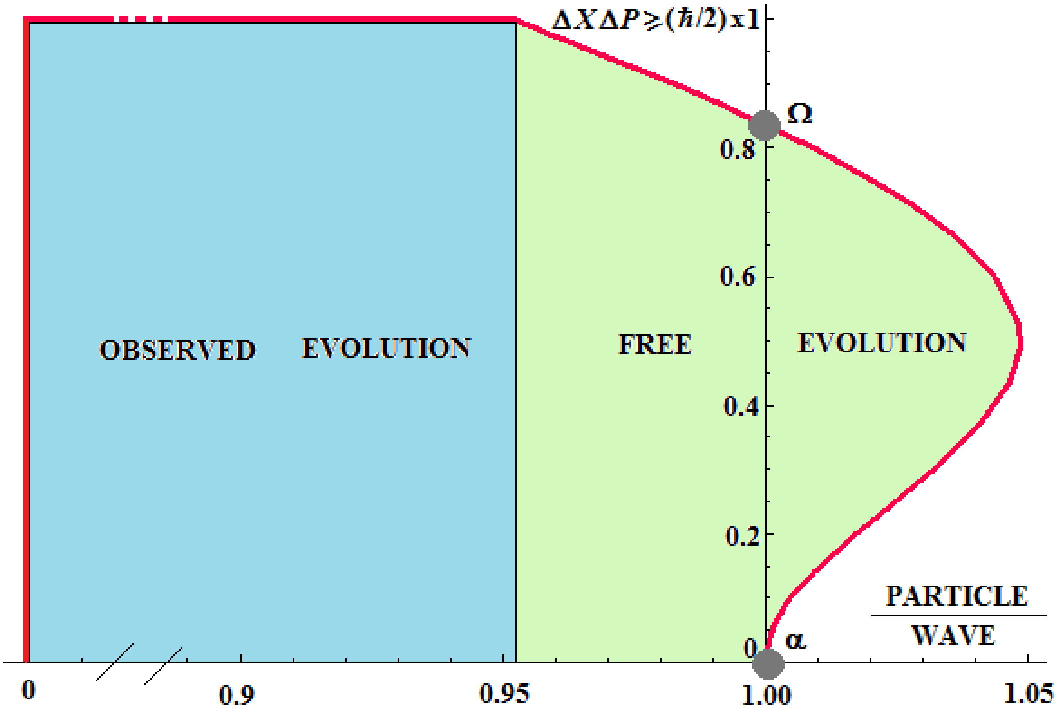

***Figure 1.*** *Complete picture of the quantum evolution (free and observed) in relation with Heisenberg indetermination [5].*

Moreover, from the general graphic (Figure 1) of quantum uncertainty is obtained even the information (or the demonstration or the analytical confirmation) regarding the fact that the matter-particle can not overcome in observed evolution the matter-wave included in the same quantum system, thus being generated the so-called function/value of the electronic localization of any type of chemical bond.

$$ELF_{P/W} = \left(\frac{Particle}{Wave}\right)_{\substack{Observed\\Evolution}} \leq 0.95$$

with the fundamental consequence of the *de plano* elimination of the situation in which a chemical bond can be eminently ionic (more particle) and with the very important message that anyway, the electrons observed in chemical bond are more under the wave form, primarily covalently manifested, exerting the chemical interaction by tunneling effects.

Thus, naturally, the next step was the elucidation of the quantum nature of the chemical bonding itself by the application both of the non-relativistic quantum processes (Schrödinger-de Broglie-Bohm) but also the relativistic one (Dirac) was concluded that in both approaches the chemical field of chemical bond can be represented by a quantum particle specific to the bonding in cause, called bondon, with the formula of mass that depends on the energy and the length of connection, between which also exists a relation of closing of Heisenberg type, generalized, as shown in Figure 2.

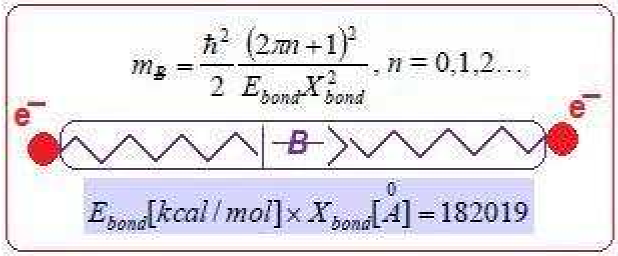

***Figure 2.*** *The representation of the chemical bond by the quantum particle called bondon, with afferent mass, and the Heisenberg principle associated in the bonding [6].*

This new fundamental result allowed the further consideration of the chemical bonding through the bondons, as being in fact a special realization of the field and of the theory of bosonic condensation (Bose-Einstein) in the area of interaction of the atoms-in-molecule. In this new context, was evaluated the bosonic hardness of bondonic type [8-10]

$$g = \left.\frac{4\pi a_B \hbar^2}{m_B}\right|_{a_B \to R_{bond}} = 8\pi E_{bond} R_{bond}^3 = \frac{8\pi E_{bond}}{\left|\langle\psi(\mathbf{r})\rangle\right|^2}$$

and was concluded that it actually depends on the energetic information of chemical bonding but also on the so-called parameter of order that modulates in fact the condensation of the pairs of electrons in bonding and anti-bonding states, which in the paradigmatic model of the homopolar diatomic molecules (Heitler-London) were provided the analytical forms [8-10]

$$E^{\pm}_{bond-BEC-I} = -\left|\langle\psi(\mathbf{r})\rangle\right|^2 \frac{\eta_{Molec}}{8\pi}\frac{V_{11} \pm V_{12}}{H_{11} \pm H_{12}}$$

$$E^{\pm}_{bond-BEC-II} = \frac{H_{11} \pm H_{12}}{1 \pm S} + \left|\langle\psi(\mathbf{r})\rangle\right|^2 \frac{\eta_{Molec}}{8\pi}\frac{V_{11} \pm V_{12}}{H_{11} \pm H_{12}}$$

These last, have two fundamental characters with an important relevance in the further studies:

- Are reduced to the classical formulas in the absence of the parameter of order: $<\psi> \to 0$
- Depend on the chemical hardness of the formed molecule, thus the principle of reactivity being well represented also at this level of analyze.

### *3.* Was integrated the principle of chemical action in the ensemble of the principles of reactivity consecrated to the modeling of the chemical bond and binding (*papers [1,2,11,12]*).

With the aid of the concept and of the principle of chemical action, was formed the complete picture of the scenario of the reactivity and chemical binding together with the influence of electronegativity and chemical hardness, after the phenomenological sequence [1,2]:

$$\delta\chi = 0 \rightarrow \delta C_A = 0 \rightarrow \Delta\chi < 0 \rightarrow \delta\eta = 0 \rightarrow \Delta\eta > 0$$

On the other side, in the itself modeling of the chemical bond based on the influence of chemical action, was approached the most general analyze, i.e. the quantum relativistic one (Dirac) through which was identified the existence of the so-called functions of chemical binding corresponding to the bonding positive and negative state of Dirac

$$f_{\beta(\pm)}^{Dir}(\lambda,\chi) = \pm\exp\left(-2\Omega\lambda C_A\right)$$

together with the one corresponding to the anti-bonding state

$$f_{\alpha}^{Dir}(\lambda,\chi) = 1 - \Omega\lambda C_A$$

With these was fulfilled not only the modeling of the electronic bond with the individual contribution of spin, but also the effective localization of the electrons with a certain spin orientation in various areas of the chemical bond, for various chemical actions (or electronegativities), in critical regime (of maximum optimal exchange of quantum information between the involved sub-levels in the chemical bond or reaction). Such a model is shown in Figure 3.

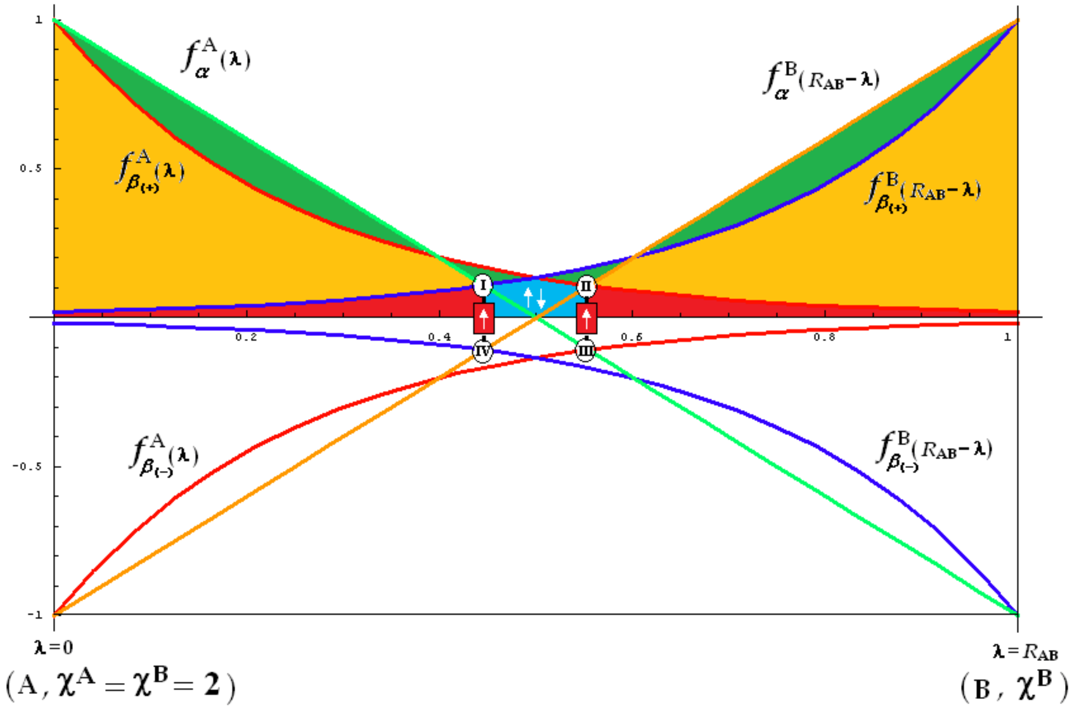

**Figure 3**. *Modeling of chemical bond by the identification of the localization of the spin coupling and of the localization of the spins of anti-bonding, in the spinorial Dirac picture in a critical case of chemical equal-actions (or electronegativities) for a chemical binar system [1].*

With this approach and modeling as demonstrated the power both conceptual and applicative of the consecrated indices of reactivity (electronegativity and chemical hardness), but also of the new concept and functional principle of the chemical action, on various levels of manifestation of the chemical interaction, and for the most general cases of the quantum evolution (aromaticity, bondons, bosonic condensation, spinorial localization).

## Conclusions and Perspectives

The 2010 stage of the present project was demonstrated as being particularly fertile in founding and promoting the principles of the conceptual and analytical tools for a general approach, but also specific to the interaction, chemical bonding and reactivity, at atomic level, molecular and macro-molecular. Essentially, the main achievements can be listed such as:

- Was formulated the scenario and the algorithm afferent to the chemical reactivity and of the chemical bond in the 3D space of electronegativity, chemical hardness and chemical action;
- Was underlined the role of the chemical action for explanation of the spin localization in chemical bonding, based on the spinorial Dirac formalism;
- Was formulated and also explained the existence of a fundamental quantum particle, specific to the chemical bonding, called bondon, able to describe the chemical interaction in the complex molecular systems, where are included also the nanosystems.

Thanks to the remarkable achievements of this first year of the complete realization of the present grant (2010-2013), the publications and the communications made, by the perspective to provide, in fact, an unitary bosonic-bondonic theory of the chemical reactivity able to describe in the most exotic conditions, especially including the bio-, eco-, pharmacological interactions, we consider the ensemble of the papers during the 2010 year of the present grant as being a real international success, being in this imperious stage necessary for the further implementations, in complex applications on the level of living substance, in the correct conceptual description and accurate computational of the bio-, eco- and pharmacological phenomena [13, 14], as like for the design, control and evaluation of the properties of toxicity of the nanomaterials.

## Written and communicated papers

1. Putz M.V. "Chemical Action Concept and Principle", *MATCH Communications in Mathematical and in Computer Chemistry*, 66(1) (**2011**) 35-63 (**ISI Impact Factor ≅ 3.2**);
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2. Putz M.V. "Electronegativity and Chemical Hardness: Different Patterns in Quantum Chemistry", *Current Physical Chemistry*, 1(2) (**2011**) 000-000;
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5. Putz M.V. "On Heisenberg Uncertainty Relationship, Its Extension, and the Quantum Issue of Wave-Particle Duality", *International Journal of Molecular Sciences*, 11(10) (**2010**) 4124-4139; DOI: 10.3390/ijms11104124 (**ISI Impact Factor ≅ 1.4**);
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6. Putz M.V. "The Bondons: The Quantum Particles of the Chemical Bond", *International Journal of Molecular Sciences*, 11(11) (**2010**) 4227-4256; DOI: 10.3390/ijms11114227 (**ISI Impact Factor ≅ 1.4**);
   ♣ URL: http://www.mdpi.com/1422-0067/11/11/4227
7. Putz M.V. "Conceptual Density Functional Theory: from Inhomogeneous Electronic Gas to Bose-Einstein Condensates", in "*CHEMICAL INFORMATION AND COMPUTATIONAL CHALLENGES IN 21$^{ST}$.*", Mihai V. Putz (Ed.), NOVA Science Publishers, Inc., New York, USA (**2011**), ISBN: 978-1-61209-712-1;

♣ URL: https://www.novapublishers.com/catalog/product_info.php?products_id=22003.

8. Putz M.V. "Hidden Side of Chemical Bond: The Bosonic Condensate", in "*ADVANCES IN CHEMISTRY RESEARCH. VOLUME 10*", James C. Taylor (Ed.), *Series „Advances in Chemistry Research”*, NOVA Science Publishers, Inc., New York, USA (**2011**), ISBN: 978-1-61324-018-2, Chapter 8;

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9. Putz M.V. „*Developing Density Functional Theory for Bose-Einstein Condensates. The Case of Chemical Bonding*”, presented to the “8th International Conference of Computational Methods in Sciences and Engineering (ICCMSE 2010)”, Kos, Greece, October 3-8, **2010**, Program and Book of Abstracts; ♣ URL: http://www.iccmse.org/ICCMSE2010/index.htm ; the extended abstract was accepted for being included in the Proceeding of the conference that will be published in the prestigious American Institute of Physics (AIP) Conference Proceeeding Series; ♣ URL: http://proceedings.aip.org/
10. Putz M.V. hold the seminar: *Towards Density Functional Theory of Bose-Einstein Condensation*; University of Szczecin (Polons), Institute of Physics, Laboratory of Molecular Physics; ♣ URL: http://wmf.univ.szczecin.pl/~fedaruk/2010-2011/Putz.html; Collaboration with the post-doc dr. Eduard Matito (http://ematito.webs.com/), regarding the completion of a study and of the afferent article on „A new definition of the softness kernel based on the exchange-correlation density”, which will be send for publication to a magazine with international impact.
11. Putz M.V. (Editor) "*QSAR & SPECTRAL-SAR IN COMPUTATIONAL ECOTOXICOLOGY*", Apple Academics, Ontario, Canada (**2011**), page 210; delivery date*: 15 October 2010*;

    ♣ URL: http://www.appleacademicpress.com
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    ♣ URL: https://www.novapublishers.com/catalog/product_info.php?products_id=22003
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14. Putz M.V., Putz A.M. "Logistic vs. W-Lambert Information in Quantum Modeling of Enzyme Kinetics", *International Journal of Chemoinformatics and Chemical Engineering*, 1(1) (**2011**) 42-60 (DOI: 10.4018/ijcce.2011010104);

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